| 1<br>2<br>3<br>4<br>5<br>6<br>7<br>8                | STEPHEN P. SWINTON (106398) J. CHRISTOPHER JACZKO (149317) COOLEY GODWARD LLP 4401 Eastgate Mall San Diego, California 92121 Telephone: (858) 550-6000 Facsimile: (858) 550-6420  R. WILLIAM BOWEN, JR. (102178) GEN-PROBE, INC. 10210 Genetic Center Drive San Diego, California 92121-4362 Telephone: (858) 410-8918 Facsimile: (858) 410-8637  Attorneys for Plaintiff |   |
|---|---|---|
| 9   | GEN-PROBE, INCORPORATED   |   |
| 10  | UNITED STAT   | TES DISTRICT COURT  |
| 11  | SOUTHERN DIS  | TRICT OF CALIFORNIA   |
| 12  |   |   |
| 13  | GEN-PROBE INCORPORATED,   | No. 99CV2668H AJB   |
| 14  | Plaintiff,  | REPLY SEPARATE STATEMENT OF UNDISPUTED                                    |
| 15  | v.  | FACTS IN SUPPORT OF PLAINTIFF GEN-PROBE INCORPORATED'S MOTION FOR PARTIAL |
| 16  | VYSIS, INC.,  | SUMMARY JUDGMENT OF NON-INFRINGEMENT UNDER THE DOCTRINE OF EQUIVALENTS    |
| 17<br>18  | Defendant.  | DATE: November 19, 2001<br>TIME: 10:30 a.m.                               |
| 19  |   | DEPT.: Court Room 1   |
| 20  |   | HONORABLE MARILYN L. HUFF   |
| 21  |   |   |
| 22  |   | en-Probe") respectfully submits that following Reply                      |
| 23  |   | apport of its Motion for Partial Summary Judgment of                      |
| 24  | Non-Infringement Under the Doctrine of Equ  | ivalents:   |
| 25  |   |   |
| 26  | ///   |   |
| 27  | ///   |   |
| 28  | ///   |   |
| COOLEY GODWARD LLP<br>ATTORNEYS AT LAW<br>SAN DIEGO | 309797 v1/SD<br>6N1H01!.DOC   | <b>99CV2668Н АЈВ</b><br>1.  |

| 1        |  |                                  |                                |
|----------|--|----------------------------------|--------------------------------|
| 2        | SAMINERVAN GERUSERGINGS<br>SAMIRERON GOVERNOON |                                  |                                |
| 3        | SUPPORT GRADIN<br>GRADING SCOTING              |                                  |                                |
| 4        | STPARATE STEATEMENTS                           | - Vysisks Opposition :           | -Genifrobystrargy              |
| 5        | 1. Vysis has previously                        | Vysis did not dispute this       | 1. Gen-Probe's proffered fact  |
| 6        | admitted that TMA is a                         | assertion in its opposition to   | is undisputed.                 |
| 7        | sequence-specific                              | Gen-Probe's April 30, 2001       |                                |
| 8        | amplification method and does                  | Motion for Partial Summary       |                                |
| 9        | not use methods of non-                        | Judgment.                        |                                |
| 10       | specific amplification.                        |                                  |                                |
| 11       | 2. All of the claims of the                    | The Court's construction of      | 2. Gen-Probe's proffered fact  |
| 12       | '338 patent incorporate an                     | the claims of the '338 patent is | is undisputed.                 |
| 13       | "amplification" element. The                   | a legal question, not a factual  |                                |
| 14       | Court's June 20th Order                        | one. Vysis contends that the     |                                |
| . 15     | confirms that each of those                    | Court's resolution of that       |                                |
| 16       | claims and incorporated                        | question of law is legally       |                                |
| 17       | amplification elements literally               | incorrect.                       |                                |
| 18       | encompasses only non-specific                  |                                  |                                |
| 19       | amplification techniques.                      |                                  |                                |
| 20       | 3. The differences between                     | Disputed. See Persing Decl.,     | 3. Dr. Persing's declaration   |
| 21       | specific amplification methods                 | ¶¶ 5-16.                         | does not state that there are  |
| 22       | and non-specific amplification                 |                                  | only insubstantial differences |
| 23       | methods are substantial.                       |                                  | between methods of specific    |
| 24       |  |                                  | amplification, such as TMA,    |
| 25       |  |                                  | and methods of non-specific    |
| 26       |  |                                  | amplification. Nothing in Dr.  |
| 27       |  |                                  | Persing's declaration would    |
| 28       |  |                                  | lead one skilled in the art to |
| WARD LLP | 309797 v1/SD                                   |                                  | OOCHAGGE A TR                  |

| 1  | LÚNDIS AUTOROMÁTICA (ÚNDISTATORA).       |                              |                                 |
|----|--|------------------------------|---------------------------------|
| 2  | SUPPORT OFFEDIN                          |                              |                                 |
| 3  | GEN-PROBE'S OPENING  SEPARATE STATEMENTS | WYSISS OPPOSITION            | A GINPROBES REPRES              |
| 4  |  |                              | reach such a conclusion.        |
| 5  |  |                              | Mullis Reply Decl. at ¶ 5.      |
| 6  |  |                              | Rather, Dr. Persing confuses    |
| 7  |  |                              | the issue by comparing          |
| 8  |  |                              | improperly target capture and   |
| 9  |  |                              | non-specific amplification to   |
| 10 |  |                              | specific amplification.         |
| 11 | 4. The methods do not                    | Disputed. See Persing Decl., | 4. Dr. Persing's declaration    |
| 12 | perform the same function in             | ¶¶ 5-16.                     | does not meaningfully address   |
| 13 | the same way to achieve the              |                              | the "triple identity" test of   |
| 14 | same result.                             |                              | whether TMA and non-            |
| 15 |  |                              | specific amplification          |
| 16 |  |                              | "perform substantially the      |
| 17 |  |                              | same function in substantially  |
| 18 |  |                              | the same way to achieve         |
| 19 |  |                              | substantially the same result." |
| 20 |  |                              | Mullis Reply Decl. at ¶ 6.      |
| 21 |  |                              | Rather, Dr. Persing confuses    |
| 22 |  |                              | the issue by comparing          |
| 23 |  |                              | improperly target capture and   |
| 24 |  |                              | noon-specific amplification to  |
| 25 |  |                              | specific amplification.         |
| 26 | 5. Gen-Probe's TMA method                | No dispute.                  | 5. Gen-Probe's proffered fact   |
| 27 | functions to exponentially               |                              | is undisputed.                  |
| 28 |  |                              |                                 |

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| 1  | UNDSRUTED AVATERIALS  TAXOTS AND LANDENHARS |                                 |                                  |
|----|---|---------------------------------|----------------------------------|
| 2  | SUPPORT CITEDIN                             |                                 |                                  |
| 3  | SEPARATE STATEMENT                          | Vysisis Opposition              | GEN-PROBES REPLAY (3)            |
| 4  | increase both the absolute and              |                                 |                                  |
| 5  | relative amount of a particular             |                                 |                                  |
| 6  | nucleic acid sequence of                    |                                 |                                  |
| 7  | interest in a mixture of nucleic            |                                 |                                  |
| 8  | acids.                                      |                                 |                                  |
| 9  | 6. In direct contrast, non-                 | In the context of the claims of | 6. Vysis does not point to any   |
| 10 | specific amplification                      | the '338 patent, the            | particular aspect of the '338    |
| 11 | functions only to increase the              | amplification step increases    | patent to support its position   |
| 12 | absolute amount of all nucleic              | both the absolute and relative  | and does not dispute the         |
| 13 | acids present in a sample and               | amount of the target nucleic    | proffered fact. Indeed, it       |
| 14 | does not increase the relative              | acid present in the tested      | appears that Vysis is confusing  |
| 15 | amount of a particular nucleic              | sample. See '338 patent.        | the issue by its preface "in the |
| 16 | acid sequence of interest.                  |                                 | context of the '338 patent."     |
| 17 |   |                                 | For purposes of the              |
| 18 |   |                                 | equivalents analysis one must    |
| 19 |   |                                 | consider the amplification       |
| 20 |   |                                 | element by itself, not the       |
| 21 |   |                                 | "invention as a whole" (e.g.     |
| 22 |   |                                 | other steps that are involved in |
| 23 |   |                                 | the claimed invention.)          |
| 24 |   |                                 | Moreover, there is no evidence   |
| 25 |   |                                 | that the combination of the      |
| 26 |   |                                 | target capture step with non-    |
| 27 |   |                                 | specific amplification methods   |
| 28 |   |                                 |                                  |

| 1  | - Tandragaradvagagare                                   |                                 |                                  |
|----|---|---------------------------------|----------------------------------|
| 2  | FACES AND EVIDENTIARY  SUPPORT CITED IN                 |                                 |                                  |
| 3  | GEN-PROBE S OPENING SEPARATE STATEMENT                  | VANISS OPPOSITION               | GEN-PROBE STREETLY               |
| 4  |   |                                 | can be used to detect small      |
| 5  |   |                                 | amounts of a target within a     |
| 6  |   |                                 | clinical sample. Mullis Reply    |
| 7  | ·   |                                 | Decl. at ¶10.                    |
| 8  |   |                                 | Moreover, Vysis' expert, Dr.     |
| 9  |   |                                 | Persing admitted that non-       |
| 10 |   |                                 | specific amplification does not  |
| 11 |   |                                 | increase the relative amount of  |
| 12 |   |                                 | target nucleic acid in a sample. |
| 13 |   |                                 | Bowen Decl., Exhibit "1" at      |
| 14 |   |                                 | 23:3-24:6. Gen-Probe's           |
| 15 |   |                                 | proffered fact is undisputed.    |
| 16 | 7. Vysis' own expert has                                | Vysis' expert has not opined    | 7. Dr. Persing's declaration     |
| 17 | admitted the differences in                             | that there is no difference     | does not state that there are    |
| 18 | function between specific                               | between specific and            | only insubstantial differences   |
| 19 | amplification and non-specific                          | nonspecific amplification       | between methods of specific      |
| 20 | amplification.  | techniques, but has the opinion | amplification, such as TMA,      |
| 21 | [N]on-specific amplification                            | that the differences are        | and methods of non-specific      |
| 22 | techniques amplify all of the nucleic acid in a sample, | insubstantial. See Persing      | amplification. Mullis Reply      |
| 23 | both target and non-target nucleic acid. Specific       | Decl. ¶¶ 5-16.                  | Decl. at ¶ 5. Moreover, Vysis'   |
| 24 | amplification techniques, in contrast, are intended to  |                                 | expert, Dr. Persing, reaffirmed  |
| 25 | amplify only the target nucleic acid.                   |                                 | his admission of the             |
| 26 |   |                                 | differences in his deposition    |
| 27 |   |                                 | testimony. Bowen Decl.,          |
| 28 |   |                                 |                                  |

| i    |  |                                       |                                  |
|------|--|---------------------------------------|----------------------------------|
| 1    | PUNDISPURATIONALITERIALES : TEXCER AND EXIDENITATES: |                                       |                                  |
| 2    | Supportation din<br>Gen-Probes Office                |                                       |                                  |
| 3    | SEPARATE STATEMENTS                                  | - Vysisis Oprosition                  | GNAROBE SRIPRY                   |
| 4    |  |                                       | Exhibit "1" at 23:3-24:6. Gen-   |
| 5    |  |                                       | Probe's proffered fact is        |
| 6    |  | · · · · · · · · · · · · · · · · · · · | undisputed.                      |
| 7    | 8. When a particular nucleic                         | No dispute.                           | 8. Gen-Probe's proffered fact    |
| 8    | acid sequence of interest is                         |                                       | is undisputed.                   |
| 9    | contained in a mixture of                            |                                       |                                  |
| 10   | nucleic acids in a clinical                          |                                       |                                  |
| 11   | sample, TMA enables a person                         |                                       |                                  |
| 12   | skilled in the art to                                |                                       |                                  |
| 13   | exponentially copy the                               |                                       |                                  |
| 14   | sequence of interest.                                |                                       |                                  |
| 15   | 9. This makes it easy to                             | No dispute.                           | 9. Gen-Probe's proffered fact    |
| 16   | determine whether or not a                           |                                       | is undisputed                    |
| 17   | pathogenic microorganism is                          |                                       |                                  |
| 18   | hiding among millions of other                       |                                       |                                  |
| 19 - | organisms in a patient sample.                       |                                       |                                  |
| 20   | 10. Specific amplification is                        | Vysis disputes that non-              | 10. Vysis' use of the phrase     |
| 21   | useful for diagnostic purposes                       | specific amplification is "not a      | "in the context of the claims of |
| 22   | even without a target capture                        | viable diagnostic method."            | the '338 patent" is erroneous    |
| 23   | step. In contrast, non-specific                      | Non-specific amplification is a       | under the so-called "all         |
| 24   | amplification is not a viable                        | viable diagnostic method when         | elements" rule. In any event,    |
| 25   | diagnostic method because it                         | used in the context of claims         | specific amplification           |
| 26   | does not increase the amount                         | of the '338 patent. May 25,           | methods, such as TMA and         |
| 27   | of a target nucleic acid relative                    | 2001 Persing Decl., ¶ 11.             | PCR, are useful for diagnostic   |
| 28   |  |                                       |                                  |

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| 1  | .: เป็นการเลของกานหลังแห่ง<br>.: :                    |                                 |                                |
|----|---|---------------------------------|--------------------------------|
| 2  | TAGTS AND LANDENHARY SUPPORT CITEDIA                  |                                 |                                |
| 3  | GEN EROBE S OPENING : SEPARATE STATEMENT              | 2- AVISIS'S OPPOSITION 2        | GENPROBESTORM                  |
| 4  | to everything else. Vysis' own                        |                                 | purposes even without a target |
| 5  | expert witness has admitted                           |                                 | capture step. Mullis Reply     |
| 6  | this important distinction:                           |                                 | Decl. at ¶ 10-12. Non-specific |
| 7  | Without the use of target                             | -                               | amplification methods, such as |
| 8  | capture prior to amplification, non-specific          |                                 | those suggested in the '338    |
| 9  | amplification would not be<br>a viable technique for  |                                 | patent, are not useful         |
| 10 | detecting target nucleic acids in a sample because,   |                                 | diagnostic methods, with or    |
| 11 | as pointed out in the quoted paragraph, non-specific  |                                 | without a target capture step. |
| 12 | amplification causes the replication of virtually any |                                 | Mullis Reply Decl. at ¶ 10-12. |
| 13 | nucleic acid sequence, including other irrelevant     |                                 | Vysis' expert, Dr. Persing,    |
| 14 | nucleic acids in the sample.                          |                                 | admitted that he is not aware  |
| 15 | ·   |                                 | of any commercially approved   |
| 16 |   |                                 | non-specific method of         |
| 17 |   |                                 | amplification. Bowen Decl.,    |
| 18 |   |                                 | Exhibit "1" at 30:8-18. Gen-   |
| 19 |   |                                 | Probe's proffered fact is      |
| 20 |   |                                 | undisputed.                    |
| 21 | 11. Therefore, Dr. Persing has                        | Vysis disputes that the quoted  | 11. Vysis does not present any |
| 22 | admitted that "without the                            | section of Dr. Persing's        | evidence to dispute the        |
| 23 | invention [i.e., the                                  | May 25, 2001 Declaration was    | admission of Dr. Persing on    |
| 24 | combination of a preliminary                          | based on the assertions in Gen- | this point. Hence, Gen-        |
| 25 | "target capture" step with                            | Probe's Undisputed Fact         | Probe's proffered fact is      |
| 26 | amplification], only specific                         | No. 10.                         | undisputed. See also Reply     |
| 27 | amplification could be used."                         |                                 | Fact No. 10.                   |
| 28 |   |                                 |                                |

| į  |   |                              |                                  |
|----|---|------------------------------|----------------------------------|
| 1  | UNDSRUHIDMAVERIAL SEEDANDENDERVERY      |                              |                                  |
| 2  | SUPPORTCHIADING                         |                              |                                  |
| 3  | GEN-PROBE'S OPENINGS SEPARATE STATEMENT | Vysis's Opposition           | GEN-PROBE-STREEDS                |
| 4  | 12. The enzymes and primers             | No dispute.                  | 12. Gen-Probe's proffered fact   |
| 5  | used in any amplification               |                              | is undisputed                    |
| 6  | process can be specific or non-         |                              |                                  |
| 7  | specific.                               |                              |                                  |
| 8  | 13. The primers used in Gen-            | No dispute.                  | 13. Gen-Probe's proffered fact   |
| 9  | Probe's specific TMA                    |                              | is undisputed                    |
| 10 | amplification method have               |                              |                                  |
| 11 | been carefully selected by              |                              |                                  |
| 12 | Gen-Probe's scientists and are          |                              |                                  |
| 13 | generally designed to bind to           | ·                            |                                  |
| 14 | specific, unique sequences in a         |                              |                                  |
| 15 | DNA or RNA molecule.                    |                              |                                  |
| 16 | 14. In amplification processes,         | Disputed. See Persing Decl., | 14. Dr. Persing's declaration    |
| 17 | sequence-specific primers and           | ¶¶ 10-16.                    | does not address this fact.      |
| 18 | enzymes such as those used in           | į                            | Rather, Dr. Persing improperly   |
| 19 | TMA play a role substantially           |                              | confuses the issue by speaking   |
| 20 | different from non-specific             |                              | in terms of the "context" of the |
| 21 | primers and enzymes.                    |                              | '338 patent. The role of         |
| 22 |   |                              | sequence-specific primers and    |
| 23 |   | ,                            | enzymes, such as those used in   |
| 24 |   |                              | MA, play a substantially         |
| 25 |   |                              | different role and achieve       |
| 26 |   |                              | substantially different results  |
| 27 |   |                              | from non-specific primers and    |
| 28 |   |                              |                                  |

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| 1  | - Frederica Vertica de la constanta de la cons |                                |                                 |
|----|--|--------------------------------|---------------------------------|
| 2  | AFACTS AND FAIDENTIARY SUPPORT CITED IN  |                                |                                 |
| 3  | GEN-PROBES OPENING SEPARATE STATEMENT  | VYSISE OPPOSITION              | GENERROBE/S'REPLY               |
| 4  |  |                                | enzymes. Mullis Reply Decl.     |
| 5  |  |                                | at ¶¶3, 12-14.                  |
| 6  | 15. This fact is well known to   | Disputed. See Persing Decl.,   | 15. Dr. Persing's declaration   |
| 7  | those of ordinary skill in the   | ¶¶ 10-16.                      | does not address this fact. See |
| 8  | art.   |                                | Mullis Reply Decl. at ¶3-7.     |
| 9  |  |                                | Gen-Probe's proffered fact is   |
| 10 |  |                                | undisputed.                     |
| 11 | 16. For example, specific  | Disputed. All nucleic acid     | 16. Persons of ordinary skill   |
| 12 | primers and enzymes can  | amplification techniques have  | in the art know and understand  |
| 13 | function together to amplify a   | some degree of nonspecificity. | that all nucleic acid           |
| 14 | target nucleic acid only if the  | See Persing Decl., ¶ 6.        | amplification techniques have   |
| 15 | specific sequence of interest  |                                | some degree of non-             |
| 16 | bound by the primer and/or   |                                | specificity. They also know     |
| 17 | recognized by the enzymes is   |                                | that this ancillary and limited |
| 18 | present in the sample.   |                                | degree of non-specificity is    |
| 19 |  |                                | immaterial to determining       |
| 20 |  |                                | whether specific amplification  |
| 21 |  |                                | techniques are equivalent to    |
| 22 |  |                                | non-specific amplification.     |
| 23 |  | ·                              | When persons of ordinary skill  |
| 24 |  | ,                              | in the art employ methods of    |
| 25 |  |                                | sequence-specific               |
| 26 |  |                                | amplification, such as TMA      |
| 27 |  |                                | and PCR, those methods are      |
| 28 |  |                                |                                 |

| 1  | TATERYA VALER DESIGNED                    |                    |                                  |
|----|---|--------------------|----------------------------------|
| 2  | FACTS AND LYDDENHARY SURFORT CHEDIN       |                    |                                  |
| 3  | AGEN-PROBE'S OPENING SEPARATE STATEMENT 3 | Vysis's Opposition | GENEROBERSREPLY                  |
| 4  |   |                    | extremely specific as            |
| 5  |   |                    | compared with amplification      |
| 6  |   |                    | using random hexamer primers     |
| 7  |   |                    | and non-specific enzymes.        |
| 8. |   |                    | The difference in specificity is |
| 9  |   |                    | like the difference between      |
| 10 |   |                    | night and day. PCR and TMA       |
| 11 |   |                    | are both 1 million times more    |
| 12 |   |                    | specific than any non-specific   |
| 13 |   |                    | amplification system, and the    |
| 14 |   |                    | consequences of this             |
| 15 |   |                    | difference are both substantial  |
| 16 |   |                    | and absolute. The fact that      |
| 17 |   |                    | TMA and PCR may result in        |
| 18 |   |                    | some very limited amount of      |
| 19 |   |                    | amplification of non-target      |
| 20 |   |                    | sequences does not render        |
| 21 |   |                    | those sequence-specific          |
| 22 | ·   |                    | methods the equivalent of non-   |
| 23 | ·   |                    | specific amplification methods   |
| 24 |   |                    | with random hexamer primers      |
| 25 |   |                    | and non-specific enzymes,        |
| 26 |   |                    | which are deliberately           |
| 27 |   |                    | designed to be totally non-      |
| 28 |   | ·                  |                                  |

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| 1  | : AUNDISEUTODMAGERIALS               |                   |                                 |
|----|--------------------------------------|-------------------|---------------------------------|
| 2  | TAGINAND LAIDENHARY SUPPORT CITED IN |                   |                                 |
| 3  | GEN-PROBE SOPENING 27                | AVSIS SEOTROSHION | GEN-PROBE'S REPLY               |
| 4  |                                      |                   | specific. Mullis Reply Decl. at |
| 5  |                                      |                   | ¶¶7-8.                          |
| 6  | 17. By contrast, non-specific        | No dispute.       | 17. Gen-Probe's proffered fact  |
| 7  | primers and enzymes will             |                   | is undisputed                   |
| 8  | amplify any and all sequences        |                   |                                 |
| 9  | present in the sample.               |                   |                                 |
| 10 | 18. The random primers will          | No dispute.       | 18. Gen-Probe's proffered fact  |
| 11 | bind to all of the sequences in      |                   | is undisputed                   |
| 12 | the sample and non-specific          |                   |                                 |
| 13 | replication enzymes will             |                   |                                 |
| 14 | catalyze DNA synthesis at            |                   |                                 |
| 15 | points throughout the entire         |                   |                                 |
| 16 | lengths of the nucleic acid          |                   |                                 |
| 17 | molecules present without            |                   |                                 |
| 18 | regard to sequence.                  |                   |                                 |
| 19 | 19. In its TMA method, Gen-          | No dispute.       | 19. Gen-Probe's proffered fact  |
| 20 | Probe uses two amplification         |                   | is undisputed                   |
| 21 | enzymes that depend upon the         |                   |                                 |
| 22 | presence of specific primers.        |                   |                                 |
| 23 | 20. One of these enzymes is          | No dispute.       | 20. Gen-Probe's proffered fact  |
| 24 | reverse transcriptase ("RT").        |                   | is undisputed                   |
| 25 | 21. RT is a DNA polymerase           | No dispute.       | 21. Gen-Probe's proffered fact  |
| 26 | that produces a                      |                   | is undisputed                   |
| 27 | complementary DNA strand             |                   |                                 |
| 28 |                                      |                   |                                 |

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| 1   | - ANGERUNMERURAUF.                           |                                |                                  |
|-----|--|--------------------------------|----------------------------------|
| 2   | SUPPORT CITED IN                             |                                |                                  |
| 3   | GEN-PROBE'S OPENING E<br>SEPARATE STATEMENTS | Vysis's Opposition :           | GENEPROBESTRUMY                  |
| 4   | copy of a single-stranded RNA                |                                |                                  |
| 5   | or DNA that has a bound                      |                                |                                  |
| 6   | primer.                                      |                                |                                  |
| 7   | 22. In TMA, RT produces                      | No dispute.                    | 22. Gen-Probe's proffered fact   |
| 8   | complementary DNA from the                   |                                | is undisputed                    |
| 9   | target nucleic acids (or their               |                                |                                  |
| 10  | complementary strands) only                  |                                |                                  |
| 11  | if the sequence-specific                     |                                |                                  |
| 12  | primers first bind to a single               |                                |                                  |
| 13  | strand of RNA or DNA.                        |                                |                                  |
| 14  | 23. If the target organism is                | Disputed. All nucleic acid     | 23. Persons of ordinary          |
| 15  | not present in the sample, the               | amplification techniques have  | skill in the art know and        |
| 16  | primers will be unable to bind               | some degree of nonspecificity. | understand that all nucleic acid |
| 17  | to the captured sequence and                 | See Persing Decl., ¶ 6.        | amplification techniques have    |
| 18  | the RT will not initiate                     |                                | some degree of non-              |
| 19  | synthesis.                                   |                                | specificity. Mullis Reply        |
| .20 |  |                                | Decl. at ¶¶ 7-8. The non-        |
| 21  |  |                                | specific products of PCR and     |
| 22  |  |                                | TMA do not affect the overall    |
| 23  |  |                                | specificity of the processes.    |
| 24  |  |                                | The primary product of           |
| 25  |  |                                | specific amplification is        |
| 26  |  |                                | identified by its precisely      |
| 27  |  |                                | defined length and the           |
| 28  |  |                                |                                  |

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| 1  | * ANDERSON (NOTERNAL)                      |                   |                                  |
|----|--|-------------------|----------------------------------|
| 2  | FACTS AND EVIDENTIARY SUPPORT GIFTED IN    |                   |                                  |
| 3  | S GEN-PROBES OPENING  SEPARATE STATEMENT * | Vysise Opposition | GENEROBESKUPAY                   |
| 4  |  |                   | presence of amplified internal   |
| 5  |  | -                 | target sequences. Spuriously     |
| 6  |  |                   | amplified sequences, when        |
| 7  |  |                   | they occur, are only rarely the  |
| 8  |  |                   | same size as the target-specific |
| 9  |  |                   | product. Furthermore,            |
| 10 |  | 2                 | spuriously amplified             |
| 11 |  |                   | sequences, when they occur,      |
| 12 | ·  | ·                 | do not contain internal          |
| 13 |  |                   | sequences that are homologous    |
| 14 |  |                   | to target-specific hybridization |
| 15 |  |                   | probes. Therefore, it is easy to |
| 16 |  |                   | distinguish the spuriously-      |
| 17 |  |                   | amplified products. Mullis       |
| 18 |  |                   | Reply Decl. at ¶ 9.              |
| 19 |  |                   |                                  |
| 20 | 24. Another specific primer                | No dispute.       | 24. Gen-Probe's proffered fact   |
| 21 | used in Gen-Probe's method                 |                   | is undisputed                    |
| 22 | also includes a specific                   |                   |                                  |
| 23 | "promoter" sequence that is                |                   |                                  |
| 24 | recognized by another enzyme               |                   |                                  |
| 25 | ("T7 RNA polymerase") that                 |                   |                                  |
| 26 | binds specifically to that                 |                   |                                  |
| 27 | promoter sequence to produce               |                   |                                  |
| 28 |  |                   |                                  |

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|    |  | er processor and a state of the |                                 |
|----|--|--|---------------------------------|
| 1  | CONTRACTOR AND ANALYSIS OF THE STREET OF THE |  |                                 |
| 2  | SUPPOR CHIEDIA<br>GENEROSPRODUNG   |  |                                 |
| 3  | SEPARATIES PATEMENT  | VANISS OPPOSITION S  | GEN-PROBES REPLY                |
| 4  | many RNA copies by   |  |                                 |
| 5  | transcription.   |  |                                 |
| 6  | 25. A function "T7 promoter"   | Disputed. All nucleic acid   | 25. Vysis' Opposition does      |
| 7  | is formed in the course of the   | amplification techniques have  | not address this fact. See Gen- |
| 8  | TMA process if, and only if,   | some degree of nonspecificity.   | Probe's Reply Undisputed        |
| 9  | (1) the primer finds and binds   | See Persing Decl., ¶ 6.  | Facts Nos. 16 and 23.           |
| 10 | to its complementary target  |  |                                 |
| 11 | sequence in the captured target  |  |                                 |
| 12 | molecule so that the target  |  |                                 |
| 13 | sequence is copied by reverse  |  |                                 |
| 14 | transcriptase and (2) the  |  |                                 |
| 15 | second primer binds to the   |  |                                 |
| 16 | newly synthesized DNA and  |  |                                 |
| 17 | DNA polymerase makes the   |  |                                 |
| 18 | complementary DNA strand.  |  |                                 |
| 19 | 26. If this double-stranded,   | No dispute.  | 26. Gen-Probe's proffered fact  |
| 20 | and hence functional, T7   |  | is undisputed                   |
| 21 | promoter is formed as a result   |  |                                 |
| 22 | of these two primer binding  |  |                                 |
| 23 | and extension processes, then  |  | ·                               |
| 24 | the T7 RNA polymerase used   |  |                                 |
| 25 | in Gen-Probe's HIV/HCV test  |  |                                 |
| 26 | will amplify the sequence  | ·  |                                 |
| 27 | attached to the T7 promoter  |  |                                 |
| 28 |  |  |                                 |

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| 1  | TABETAN MEGTICERICATE  **EVANDA GUARAN MARTINA |                                |                              |
|----|--|--------------------------------|------------------------------|
| 2  | SUPPORTECTION  |                                |                              |
| 3  | GEN-PROBES OPENING SEPARATESTATEMENT   | · COUECASO METAVA              | GEN PROBES ROLLY             |
| 4  | sequence.  |                                |                              |
| 5  | 27 The T7 RNA polymerase   | Disputed. All nucleic acid     | 27. See Gen-Probe's Reply    |
| 6  | does not amplify other   | amplification techniques have  | Undisputed Facts Nos. 16 and |
| 7  | sequences present in the   | some degree of nonspecificity. | 23.                          |
| 8  | sample because they are not  | See Persing Decl., ¶ 6.        |                              |
| 9  | attached to a T7 promoter  |                                |                              |
| 10 | sequence.  |                                |                              |
| 11 | 28. Thus, in Gen-Probe's   | Disputed. All nucleic acid     | 28. See Gen-Probe's Reply    |
| 12 | HIV/HCV test, the T7   | amplification techniques have  | Undisputed Facts Nos. 16 and |
| 13 | polymerase enzyme  | some degree of nonspecificity. | 23.                          |
| 14 | specifically recognizes the T7   | See Persing Decl., ¶ 6.        |                              |
| 15 | promoter sequence, which has   |                                |                              |
| 16 | been specifically attached to  |                                |                              |
| 17 | the target sequence by the   |                                |                              |
| 18 | binding of specific primers,   |                                |                              |
| 19 | and the T7 polymerase  |                                |                              |
| 20 | specifically amplifies only that   |                                |                              |
| 21 | sequence.  |                                |                              |
| 22 | 29. The process repeats in a   | Disputed. All nucleic acid     | 29. See Gen-Probe's Reply    |
| 23 | cyclic fashion, only amplifying  | amplification techniques have  | Undisputed Facts Nos. 16 and |
| 24 | the particular target sequence   | some degree of nonspecificity. | 23.                          |
| 25 | of interest.   | See Persing Decl., ¶ 6.        |                              |
| 26 | 30. Gen-Probe's amplification  | Disputed. All nucleic acid     | 30. See Gen-Probe's Reply    |
| 27 | method therefore safeguards  | amplification techniques have  | Undisputed Facts Nos. 16 and |
| 28 |  | 1                              |                              |

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| 1  | UNDSRUTED MATERIALS FACTS AND EVIDENHARY      |                                |                                  |
|----|---|--------------------------------|----------------------------------|
| 2  | Support Gitted IN-                            |                                |                                  |
| 3  | GEN-PROBE'S OPENING SY<br>SEPARATE STATEMENTS | YYSIS'S OPPOSITION             | GEN-PROBE'S REPLY                |
| 4  | against amplification of non-                 | some degree of nonspecificity. | 23.                              |
| 5  | target sequences and thus                     | See Persing Decl., ¶ 6.        |                                  |
| 6  | protects against false positive               |                                |                                  |
| 7  | results.                                      |                                |                                  |
| 8  | 31. TMA functions in way                      | Disputed. See Persing Decl.,   | 31. None of the statements in    |
| 9  | that is substantially different               | ¶¶ 9-16.                       | Dr. Persing's declaration is     |
| 10 | than the way in which non-                    |                                | material to considering          |
| 11 | specific amplification                        |                                | whether there are substantial    |
| 12 | functions.                                    |                                | differences between TMA and      |
| 13 |   |                                | non-specific amplification.      |
| 14 |   |                                | One of ordinary skill in the art |
| 15 |   |                                | would conclude that there are    |
| 16 |   |                                | substantial differences          |
| 17 |   |                                | between Gen-Probe's TMA          |
| 18 |   |                                | method and the non-specific      |
| 19 |   |                                | amplification methods            |
| 20 |   |                                | described and claimed in the     |
| 21 |   |                                | '338 patent. Sequence-           |
| 22 |   |                                | specific amplification methods   |
| 23 |   | ·                              | such as TMA do not perform       |
| 24 |   |                                | substantially the same function  |
| 25 |   |                                | in substantially the same way    |
| 26 |   |                                | to achieve substantially the     |
| 27 |   |                                | same result as non-specific      |
| 28 |   |                                |                                  |

| ł  |  |  |                             |
|----|--|--|-----------------------------|
| 1  | AUNDISTRIANA AND REAL TO A STREET  |  |                             |
| 2  | FACTS AND EVIDENTIARYA<br>SEE SUPPORT CITED IN SE  |  |                             |
| 3  | GEN-PROBES OPENING & SEPARATE STATEMENTE   | WSISE OPPOSITION   | Gen Problem in              |
| 4  | A section of a production of the section of the sec | Section of the Company of the Compan | methods of amplification.   |
| 5  |  |  | Mullis Reply Decl. at ¶ 16. |
| 6  | 32. Specific amplification   | Disputed. Specific   | 32. Gen-Probe's proffered   |
| 7  | methods commonly achieve   | amplification methods can  | fact remains undisputed.    |
| 8  | exponential amplification of   | achieve either linear or   | Vysis has conducted its     |
| 9  | the target sequence, as  | exponential amplification,   | discovery and cites to no   |
| 10 | compared with linear   | depending on the reaction  | evidence to refute the      |
| 11 | amplification.   | conditions and the techniques  | proffered fact.             |
| 12 |  | employed. Vysis requires   |                             |
| 13 |  | discovery from Gen-Probe's   |                             |
| 14 |  | expert to provide further  |                             |
| 15 |  | support for its dispute of this  |                             |
| 16 |  | fact.  |                             |
| 17 | 33. Sustained, significant,  | Disputed. Specific   | 33. Gen-Probe's proffered   |
| 18 | exponential amplification is a   | amplification methods can  | fact remains undisputed.    |
| 19 | hallmark of specific   | achieve either linear or   | Vysis has conducted its     |
| 20 | amplification methods.   | exponential amplification,   | discovery and cites to no   |
| 21 |  | depending on the reaction  | evidence to refute the      |
| 22 |  | conditions and the techniques  | proffered fact.             |
| 23 |  | employed. Vysis requires   |                             |
| 24 |  | discovery from Gen-Probe's   |                             |
| 25 |  | expert to provide further  |                             |
| 26 |  | support for its dispute of this  |                             |
| 27 |  | fact.  |                             |
| 28 |  |  |                             |

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| 1  | FAREGRANGERGERGER                            |                                  |                                  |
|----|--|----------------------------------|----------------------------------|
| 2  | SUPPORT GUEDAN                               |                                  |                                  |
| 3  | GÉN-PROBL'S OPENING SE<br>SEPARATÉ STATEMENT | VASIS'S OPPOSITION.              | GEN-PROBE'S REPLY                |
| 4  | 34. In contrast, the non-                    | No dispute.                      | 34. Gen-Probe's proffered        |
| 5  | specific amplification methods               |                                  | fact is undisputed.              |
| 6  | of Examples 4 and 5 of the                   |                                  |                                  |
| 7  | '338 patent admittedly achieve               |                                  |                                  |
| 8  | only linear amplification, not               |                                  |                                  |
| 9  | exponential amplification.                   |                                  |                                  |
| 10 | 35. The non-specific                         | Disputed. Example 6 of the       | 35. Gen-Probe's proffered        |
| 11 | amplification methods of                     | '338 patent discloses a          | fact remains undisputed.         |
| 12 | Examples 5 and 6 also cannot                 | technique for achieving          | Vysis submits no evidence to     |
| 13 | achieve exponential                          | exponential amplification of a   | refute that of Dr. Mullis in his |
| 14 | amplification. Because                       | target nucleic acid. ('338       | September 26, 2001               |
| 15 | random primers bind at                       | patent, col. 31, line 55 to col. | Declaration at ¶41.              |
| 16 | various places along the                     | 32, line 7.)                     |                                  |
| 17 | nucleic acids present in the                 |                                  |                                  |
| 18 | sample, the products of                      |                                  |                                  |
| 19 | amplification are fragmented.                |                                  |                                  |
| 20 | 36. If these products were                   | Disputed.                        | 36. Vysis submits no             |
| 21 | then subjected to another                    |                                  | evidentiary support for its      |
| 22 | round of non-specific                        |                                  | claimed "dispute". Hence,        |
| 23 | amplification, the resulting                 |                                  | Gen-Probe's proffered fact       |
| 24 | products would be smaller                    |                                  | remains undisputed.              |
| 25 | still.                                       |                                  |                                  |
| 26 | 37. Multiple rounds of non-                  | Disputed. Vysis requires         | 37. Vysis submits no             |
| 27 | specific amplification thus                  | discovery from Gen-Probe's       | evidentiary support for its      |
| 28 |  |                                  |                                  |

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| 1  | ETUNDARINA DI YAYARINE E               |                                 |                                  |
|----|--|---------------------------------|----------------------------------|
| 2  | FACTS AND EXIDENTIARY SUPPORT GIVED IN |                                 |                                  |
| 3  | : GEN-PROBEROPANING -                  |                                 | GINPRODESROPAS                   |
| 4  | diminish rapidly in efficiency,        | expert to provide further       | claimed "dispute". Hence,        |
| 5  |  | •                               | •                                |
| 6  | whereas multiple rounds of             | support for its dispute of this | Gen-Probe's proffered fact       |
|    | specific amplification produce         | fact.                           | remains undisputed.              |
| 7  | extraordinarily large amounts          |                                 |                                  |
| 8  | of full size product nucleic           |                                 |                                  |
| 9  | acids in very short periods of         |                                 |                                  |
| 10 | time.                                  | ·                               |                                  |
| 11 | 38. Non-specific amplification         | No dispute.                     | 38. Gen-Probe's proffered        |
| 12 | using random hexamer primers           |                                 | fact is undisputed.              |
| 13 | results in fragmented nucleic          |                                 | •                                |
| 14 | acids, each of which contains          |                                 |                                  |
| 15 | the random sequences present           |                                 |                                  |
| 16 | in the primers.                        |                                 |                                  |
| 17 | 39. The resulting products are         | Disputed.                       | 39. Vysis submits no             |
| 18 | thus heterogeneous and have            |                                 | evidentiary support for its      |
| 19 | undefined composition.                 |                                 | claimed "dispute". Hence,        |
| 20 | _                                      |                                 | Gen-Probe's proffered fact       |
| 21 |  |                                 | remains undisputed.              |
| 22 | 40. Such nucleic acids are             | Disputed. In the context of the | 40. Vysis attempt to preface     |
| 23 | unsuitable for most of the             | claimed invention, non-         | its position with the phrase "in |
| 24 | purposes for which                     | specific amplification          | the context of the claimed       |
| 25 | homogeneous, specifically              | techniques can amplify target   | invention" is improper and in    |
| 26 | amplified nucleic acids of             | nucleic acids in a manner       | violation of the "all elements"  |
| 27 | known composition are                  | sufficient to permit their      | rule. In any event, non-         |
| 28 | 1                                      |                                 |                                  |

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| 1  | entréénégetentement.          |                              |                                  |
|----|-------------------------------|------------------------------|----------------------------------|
| 2  | STURFORT CHTTOTIS:            |                              |                                  |
| 3  | GERGERON GOPPANINGS           | - NONTROS OPPOSITION -       | GENEPROBES RURAY                 |
| 4  | employed.                     | detection as part of a       | specific amplification           |
| 5  |                               | diagnostic assay.            | methods, such as those           |
| 6  |                               |                              | suggested in the '338 patent,    |
| 7  |                               |                              | are not useful diagnostic        |
| 8  |                               |                              | methods, with or without a       |
| 9  |                               |                              | target capture step. Mullis      |
| 10 |                               |                              | Reply Decl. at ¶ 10.             |
| 11 | 41. As a result, Gen-Probe's  | Disputed. See Persing Decl., | 41. Dr. Persing's declaration    |
| 12 | TMA method also does not      | ¶¶ 9-16.                     | suggests that TMA and the        |
| 13 | yield the same result as that |                              | non-specific amplification       |
| 14 | obtained with non-specific    |                              | method of Example 5 of the       |
| 15 | amplification.                |                              | '338 patent both result in the   |
| 16 |                               |                              | creation of a double-stranded    |
| 17 |                               |                              | DNA, and this double-stranded    |
| 18 |                               |                              | DNA constitutes the "same        |
| 19 |                               |                              | result" from each process.       |
| 20 |                               |                              | This statement is not true. The  |
| 21 |                               |                              | mere fact that both products     |
| 22 |                               |                              | are double-stranded DNA is       |
| 23 |                               |                              | immaterial to one skilled in the |
| 24 |                               |                              | art. What is important is the    |
| 25 |                               |                              | content of the double-stranded   |
| 26 |                               |                              | DNA. The double-stranded         |
| 27 |                               |                              | product of the amplification     |
| 28 |                               |                              |                                  |

| 1  | and district and the state of t |                       |                                 |
|----|--|-----------------------|---------------------------------|
| 2  | EVACINAVALENDENTENY<br>SURFORMETTARE   |                       |                                 |
| 3  | GEN-PROBLES OPENING :=<br>SEPARATE STATEMENT:  | VAVSIS'S FOR POSITION | GENEROB SERVEY                  |
| 4  |  |                       | method of Example 5 would       |
| 5  |  |                       | be a heterogeneous collection   |
| 6  |  |                       | of fragments containing a       |
| 7  |  |                       | mixture of sequences present    |
| 8  |  |                       | in the original sample.         |
| 9  |  |                       | Whether or not the collection   |
| 10 |  |                       | of fragments contains any       |
| 11 |  |                       | sequences of a specific target  |
| 12 |  |                       | is unknown. In contrast, PCR    |
| 13 |  |                       | and TMA produce discrete        |
| 14 |  |                       | products of known size and      |
| 15 |  |                       | composition. Both the           |
| 16 |  |                       | absolute and relative amounts   |
| 17 |  |                       | of the specific target sequence |
| 18 |  |                       | are increased millions-fold,    |
| 19 |  |                       | allowing the detection of even  |
| 20 |  |                       | a single molecule of target     |
| 21 |  |                       | within millions of molecules    |
| 22 |  |                       | of non-target sequence. Mullis  |
| 23 |  |                       | Reply Decl. at ¶ 11. Vysis'     |
| 24 |  |                       | expert, Dr. Persing, admitted   |
| 25 |  |                       | that even employing the         |
| 26 |  |                       | method of Example 5's           |
| 27 |  |                       | "alternative" capture probe     |
| 28 |  |                       |                                 |

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| 1  | - PAREMAN PROGRESSIONES                    |                                |                              |
|----|--|--------------------------------|------------------------------|
| 2  | TEACHEAND WIDDNIE AND STREET               |                                |                              |
| 3  | GÉN-PROBES OPENING S<br>SEPARATE STATEMENT | = ZOURGGGBBBBBW                | GENERROBE(SROPK)             |
| 4  |  |                                | method could result in non-  |
| 5  |  |                                | specific replication of DNA. |
| 6  |  |                                | Bowen Decl., Exhibit "1" at  |
| 7  |  |                                | ¶114:20-24.                  |
| 8  | 42. The Court has previously               | Vysis disputes the implication | 42. Vysis submits no         |
| 9  | noted that the specification of            | that specific amplification    | evidentiary support for its  |
| 10 | the '338 patent contains no                | techniques are excluded from   | claimed "dispute". Hence,    |
| 11 | reference to any specific                  | the claims of the '338 patent. | Gen-Probe's proffered fact   |
| 12 | amplification techniques. To               |                                | remains undisputed.          |
| 13 | the contrary, the specification            |                                |                              |
| 14 | clearly suggests that the                  |                                |                              |
| 15 | claimed amplification                      |                                |                              |
| 16 | techniques of the invention                |                                |                              |
| 17 | don't require the use of                   |                                |                              |
| 18 | specific primers necessary for             |                                |                              |
| 19 | specific amplification.                    |                                |                              |
| 20 | 43. This absence in the '338               | Vysis disputes there is an     | 43. Vysis submits no         |
| 21 | patent of any disclosure of                | absence of any disclosure of   | evidentiary support for its  |
| 22 | specific amplification                     | specific amplification in the  | claimed "dispute". Hence,    |
| 23 | techniques was not accidental              | '338 patent. Vysis does not    | Gen-Probe's proffered fact   |
| 24 | or unintended. To the                      | dispute that Dr. Lawrie made   | remains undisputed.          |
| 25 | contrary, Gene-Trak Systems,               | the quoted statements in his   |                              |
| 26 | Vysis' predecessor-in-interest,            | deposition, but disputes the   |                              |
| 27 | and its employed inventors                 | relevance of those statements  |                              |
| 28 |  |                                |                              |

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| 1  | . Indisamedavijadia  |                          |                |
|----|--|--------------------------|----------------|
| 2  | EAGNANDEVIDENTIALY<br>SUPPORT GUIDIN   |                          |                |
| 3  | GENERROBE SOPENING SEPARATE STATEMENTS   | · Wysis's Opposition     | GENEROBESROPAY |
| 4  | were well aware of the specific  | to the determination of  |                |
| 5  | amplification techniques such  | infringement under the   |                |
| 6  | as PCR. In fact, the admitted  | doctrine of equivalents. |                |
| 7  | focus of the inventors' effort   |                          |                |
| 8  | leading to the disclosure in the   | •                        |                |
| 9  | '338 patent was to find  |                          |                |
| 10 | something "different" from   |                          |                |
| 11 | specific amplification. For  |                          |                |
| 12 | example, inventor Jon Lawrie   |                          |                |
| 13 | testified that the patent was  |                          |                |
| 14 | meant to cover new   |                          |                |
| 15 | amplification methods using  |                          |                |
| 16 | non-specific primers, not  |                          |                |
| 17 | already-known methods such   |                          |                |
| 18 | as PCR:  |                          |                |
| 19 | Q. Can you recall any  |                          |                |
| 20 | reason that a reference to PCR might have been                                   |                          |                |
| 21 | intentionally omitted from the patent application?                               |                          |                |
| 22 | A. Yes   |                          |                |
| 23 | Q. If there's no reference   |                          |                |
| 24 | in the ['338] patent to<br>combining target capture<br>with PCR, do you have any |                          |                |
| 25 | explanation as to why it is not there?   |                          |                |
| 26 | A. I believe that it was a   |                          |                |
| 27 | separate, the thought behind this [referring to the                              |                          |                |
| 28 | in ocimic and freighting to me.  | l                        |                |

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|         | 1  |                               |                           |
|---------|--|-------------------------------|---------------------------|
| 1       | Zaundinatanayyanangi.  |                               |                           |
| 2       | TAYON AND EXIDENTIALLY.  |                               |                           |
| 3       | GENEROBUS OPENING = -<br>SEPATATE STATEMENT                            | - Wysisia Opposition          | GEN PROBES RIPER          |
| 4       | '338 patent] was coming up<br>with new methods of                      |                               |                           |
| 5       | amplification, not old ones.   |                               |                           |
| 6       | Q. For the purposes of what you just said you                          |                               |                           |
| 7       | classify PCR as an old method of amplification?                        |                               |                           |
| 8       | A. PCR itself was  |                               |                           |
| 9       | described in the patent, issued patent [e.g., it was an "old" method]. |                               |                           |
| 11      | Q. And your understanding of the 338 patent was that it                |                               |                           |
| 12      | was directed to other methods of amplification?                        |                               |                           |
| 13      | A. The, it was, it was   |                               |                           |
| 14      | directed to the methods disclosed by, you know, the                    |                               |                           |
| 15      | methods separate from PCR.   |                               |                           |
| 16      | 44. Inventor King also stated  | Vysis does not dispute that   | 44. Gen-Probe's proffered |
| 17      | the inventors' purpose and also  | Dr. King made the quoted      | fact is undisputed.       |
| 18      | distinguished non-specific   | statements in his deposition, |                           |
| 19      | amplification from PCR:  | but disputes the relevance of |                           |
| 20   21 | Q. From a high level perspective, what were the                        | those statements to the       |                           |
| 22      | discussion topics addressed during this meeting?                       | determination of infringement |                           |
| 23      | A. I think that at the   | under the doctrine of         |                           |
| 24      | highest level we were looking for amplification                        | equivalents.                  |                           |
| 25      | methods that did not involve PCR amplification.                        |                               |                           |
| 26      | (King Depo. At 45: 10-15   |                               |                           |
| 27      | (emphasis added).)   |                               |                           |
| 28      | Q. Okay. So the purpose the general purpose of                         |                               |                           |
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| 1  | ANDRIMANA WARRAW   |                     |                                |
|--|--|---------------------|--------------------------------|
| 2  | HACTS AND EVID STURYS  |                     |                                |
| 3  | GEN-PROBE'S OPENING SEPARATE STATEMENT   | Vaysis's Opposition | Generoessrowy                  |
| 4  | the discussion as I understand it that took  |                     |                                |
| 5  | place at Gene-Trak among<br>the four doctors was to  |                     |                                |
| 6  | identify in general identify an amplification  |                     |                                |
| 7  | technique that would amplify low concentrations  |                     |                                |
| 8  | of target nucleic acids in a sample, correct?  |                     |                                |
| 9  | A. Yes.  |                     |                                |
| 10   | Q. And as I understand   |                     |                                |
| . 11   | your testimony, you wanted to find a technique <i>that was</i>   |                     |                                |
| 12   | different from PCR, correct?   |                     | ·                              |
| 13   | A. Yes.  |                     |                                |
| 14   | 45. As this testimony  | No dispute.         | 45. Gen-Probe's proffered fact |
| 15   | suggests, PCR was well   |                     | is undisputed.                 |
| 16   | known to the inventors and the   |                     |                                |
| 17   | scientific community at large.   |                     |                                |
| 18   |  |                     |                                |
|  | Dr. Kary Mullis invented PCR   |                     |                                |
| 19   | Dr. Kary Mullis invented PCR in 1983, for which he received  |                     |                                |
| 19<br>20   |  |                     |                                |
| 19<br>20<br>21                                   | in 1983, for which he received   |                     |                                |
| 19<br>20<br>21<br>22                             | in 1983, for which he received the Nobel Prize in Chemistry.   |                     |                                |
| 19<br>20<br>21<br>22<br>23                       | in 1983, for which he received<br>the Nobel Prize in Chemistry.<br>Dr. Mullis and his colleagues   |                     |                                |
| 19<br>20<br>21<br>22<br>23<br>24                 | in 1983, for which he received<br>the Nobel Prize in Chemistry.<br>Dr. Mullis and his colleagues<br>publicly described PCR at a  | ·                   |                                |
| 19<br>20<br>21<br>22<br>23<br>24                 | in 1983, for which he received the Nobel Prize in Chemistry.  Dr. Mullis and his colleagues publicly described PCR at a scientific meeting in the  |                     |                                |
| 19<br>20<br>21<br>22<br>23<br>24<br><br>25<br>26 | in 1983, for which he received the Nobel Prize in Chemistry.  Dr. Mullis and his colleagues publicly described PCR at a scientific meeting in the summer of 1985 and published                             |                     | ·                              |
| 19<br>20<br>21<br>22<br>23<br>24                 | in 1983, for which he received the Nobel Prize in Chemistry.  Dr. Mullis and his colleagues publicly described PCR at a scientific meeting in the summer of 1985 and published their discovery in December | No dispute.         | 46. Gen-Probe's proffered      |

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| 1  | TANTINE TO RECORD THE STATE OF |                                |                                |
|----|---|--------------------------------|--------------------------------|
| 2  | ACCUTO PROBLEM - :  |                                |                                |
| 3  | GEN-PROBL'S OPENING. SEPARATESTATEMENT  | Vysisks Opposition             | GINEROBESRIDAY                 |
| 4  | Trak's Director of Business   |                                | fact is undisputed.            |
| 5  | Development and Licensing,  |                                |                                |
| 6  | admits that, within the   |                                |                                |
| 7  | scientific community, PCR   |                                | ·                              |
| 8  | was immediately "big news."   |                                |                                |
| 9  | 47. One of the reasons that the   | No dispute.                    | 47. Gen-Probe's proffered fact |
| 10 | '338 inventors sought to find   | ;                              | is undisputed.                 |
| 11 | something "different" from  |                                |                                |
| 12 | specific amplification  |                                |                                |
| 13 | techniques such as PCR was  |                                |                                |
| 14 | due to Gene Trak's concern  |                                |                                |
| 15 | that it could not obtain a  |                                |                                |
| 16 | license from Cetus Corp. to   |                                |                                |
| 17 | use PCR. Cetus Corporation,   |                                |                                |
| 18 | which employed Dr. Mullis,  |                                |                                |
| 19 | originally owned the rights to  |                                |                                |
| 20 | PCR. Gene-Trak sought a   |                                |                                |
| 21 | license from Cetus, but its   |                                |                                |
| 22 | requests were rejected.   |                                |                                |
| 23 | 48. The view of the   | Vysis disputes the statement   | 48. Vysis' expert, Dr.         |
| 24 | fundamental difference  | that there is a "fundamental   | Persing's declaration does not |
| 25 | between non-specific and  | difference between non-        | address this fact. Rather, Dr. |
| 26 | specific amplification  | specific and specific          | Persing improperly confuses    |
| 27 | techniques was shared not only  | amplification techniques." See | the issue by referring to the  |
| 28 |   | ,                              |                                |

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| 1  | SANDERBUNDAN KORDINIST SANDERBUNDING SA            |                                |                                |  |
|----|--|--------------------------------|--------------------------------|--|
| 2  | Supportendon ::                                    |                                |                                |  |
| 3  | GEN-PROBE'S OPENING SEPARATE STATEMENT:            | Vysis's Opposition             | GENERROBE'S REPLY              |  |
| 4  | between the inventors but with                     | Persing Decl., ¶¶ 5 -16. Vysis | "context" of the '338 patent   |  |
| 5  | Gene-Trak scientific                               | also disputes that the         | rather than the element of     |  |
| 6  | management as well. In                             | independent claims of the '338 | amplifying. Nothing in Dr.     |  |
| 7  | particular, in a letter he wrote                   | patent ever recited non-       | Persing's declaration refutes  |  |
| 8  | in 1989, Dr. Richards,                             | specific primers or promoters. | the testimony cited by Gen-    |  |
| 9  | pointedly contrasted the '338                      |                                | Probe in support of this fact  |  |
| 10 | patent's method of non-                            |                                | and it remains undisputed.     |  |
| 11 | specific amplification with                        |                                | Moreover, Dr. Persing          |  |
| 12 | other known specific methods                       |                                | admitted in his deposition     |  |
| 13 | that used specific primers or                      |                                | testimony that substantial and |  |
| 14 | promoters:   |                                | fundamental differences exist  |  |
| 15 | Cetus, Sibia/Salk,                                 |                                | between specific and non-      |  |
| 16 | Biotechnica, etc. all claim specific primers for   |                                | specific methods of            |  |
| 17 | amplification whereas the present invention claims |                                | amplification. Bowen Decl.,    |  |
| 18 | uses of the opposite, namely, non-specific         |                                | Exhibit "1" at 23:3-24:6;      |  |
| 19 | primer or promoters                                |                                | 25:19-26:21; 30:8-18; 57:8-    |  |
| 20 |  |                                | 58:18; 61:20-62:13.            |  |
| 21 | Dated: November 2, 2001                            | STEPHEN P. SW                  |                                |  |
| 22 | ·  | J. CHRISTOPHE<br>COOLEY GODV   |                                |  |
| 23 | R. WILLIAM BOWEN, JR.                              |                                |                                |  |
| 24 |  | GEN-PROBE, IN                  | NC.                            |  |
| 25 |  | 1/1                            |                                |  |
| 26 |  | Ву:                            | tophen P. Swinton              |  |
| 27 |  | Attorneys for Pla              | •                              |  |
| 28 | GEN-PROBE INCORPORATED                             |                                |                                |  |

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